K073382

510(k) Summary of Safety and Effectiveness

Plexus EBV IgG Multi-Analyte Diagnostics Catalog No. MP0500G
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Applicant	Focus Diagnostics, Inc. 10703 Progress Way Cypress, California 90630 USA
Establishment Registration No.	2023365
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Summary Date	July 17, 2008
Proprietary Name	Plexus EBV IgG Multi-Analyte Diagnostics
Generic Name	Epstein-Barr Virus Serological Assays
Classification	Class I
Predicate Devices	Diamedix EBV VCA IgG ELISA Diamedix EBV EBNA-1 IgG ELISA Diamedix EBV EA-D IgG ELISA ATHENA MULTI-LYTE EBV IGG TEST SYSTEM Focus EBV-VCA ANTIBODY (IGG) - IFA

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Device Description

Multiplexed Immunoassay for the Qualitative Detection of Human IgG Antibodies to Epstein-Barr Virus

Intended Use

Focus Diagnostics' Plexus™ EBV IgG Multi-Analyte Diagnostics test kit is intended for qualitatively detecting the presence or absence of human IgG class antibodies to viral capsid antigen (VCA), early antigen- diffuse (EA-D), and nuclear antigen (EBNA-1) of Epstein-Barr virus in human sera. The test is indicated as an aid in the diagnosis of EBV infection and EBV-associated infectious mononucleosis.

The performance of this assay has not been established for use in the diagnosis of nasopharyngeal carcinoma and Burkitt's lymphoma, for testing of immunocompromised patients, for use by a point of care facility or for use with automated equipment. This assay has not been evaluated for donor screening.

Test Principle

The Focus Diagnostics Plexus™ EBV IgG uses an Antigen Bead suspension that contains three distinct EBV antigen bead types (EA-D, VCA, & EBNA-1) and one process control bead type that fluoresce at different wavelengths and/or intensities.

The Focus Diagnostics Plexus™ EBV IgG is a three step procedure.

1. Patient sera are diluted, and the diluted sera are incubated with Antigen Beads. If EBV antibodies are present, then the antibodies bind to the corresponding antigen beads.
2. Phycoerythrin-conjugated goat Anti-human IgG (Conjugate) is added, binds to the bound EBV antibody (if present), and forms a Conjugate-EBV antibody-antigen bead sandwich.
3. Fluorescence from each distinct EBV antigen bead type is measured and compared against a Cutoff Calibrator.

Comparison of Plexus EBV VCA IgG analyte to Predicates:

Item	Device	Predicates		
Name	Plexus™ EBV IgG Multi-Analyte Diagnostics	Diamedix VCA IgG, ELISA	Athena Multi-Lyte EBV VCA IgG Test System	Focus Epstein-Barr Virus VCA IFA IgG
Similarities between Device and Predicate				
Intended use	Focus Diagnostics' Plexus™ EBV (VCA) IgG Multi-Analyte is intended for qualitatively detecting the presence or absence of human IgG class antibodies to viral capsid antigen (VCA), early antigen – diffuse pattern (EA-D), and nuclear antigen (EBNA-1) of Epstein-Barr virus (EBV) in human sera. The test is indicated as an aid in the diagnosis of EBV infection and EBV-associated infectious mononucleosis.	Diamedix Corp EBV VCA IgG ELISA is intended for the qualitative and semi-quantitative determination of IgG antibodies to Epstein-Barr Virus (recombinant) Viral Capsid Antigen (EBV-VCA IgG) in human serum by indirect enzyme immunoassay. The *Is*-EBV-VCA IgG test kit may be used in combination with other Epstein-Barr serologies, Viral Capsid Antigen (VCA) IgM, Epstein-Barr Nuclear Antigen-1 (EBNA-1) IgG and IgM, Early Antigen-Diffuse (EA-D) IgG and IgM and heterophile antibody, as an aid in the diagnosis of infectious mononucleosis (IM).	The Zeus Scientific, Inc. AtheNA Multi-Lyte® EBV IgG Test System is intended for the qualitative detection of IgG class antibody to three separate EBV Antigens (EBV-VCA gp-125, EBV-EA "total" and recombinant EBNA-1) in human serum using the AtheNA Multi-Lyte® System. The test system is intended to be used as an aid in the laboratory diagnosis of EBV-associated infectious mononucleosis and to provide epidemiological information on the disease caused by Epstein-Barr virus.	Focus Diagnostics' Epstein-Barr Virus Viral Capsid Antigens (EBV VCA) IgG Immunofluorescence Antibody (IFA) test is intended for the detection and semi-quantitation of human IgG antibodies to the viral capsid antigens (VCA) of Epstein-Barr virus in human serum as an aid in the clinical diagnosis of infectious mononucleosis.
Indications for use	The test is indicated as an aid in the diagnosis of EBV infection and EBV-associated infectious mononucleosis.	The device is indicated for use with patients with the signs and symptoms of infectious mononucleosis.	The Zeus Scientific, Inc. AtheNA Multi-Lyte EBV IgG Test System is intended for the qualitative detection of IgG class antibody to three separate EBV Antigens (EBV-	The test is indicated as an aid in the clinical diagnosis of infectious mononucleosis.

Item	Device	Predicates		
Name	**Plexus™ EBV IgG Multi-Analyte Diagnostics**	**Diamedix VCA IgG, ELISA**	**Athena Multi-Lyte EBV VCA IgG Test System**	**Focus Epstein-Barr Virus VCA IFA IgG**
			VCA, EBV-EA and EBNA-1) in human serum using the AtheNA Multi-Lyte System. The test system is intended to be used with these EBV IgG markers along with anti-EBV VCA IgM to aid in the laboratory diagnosis of EBV-associated infectious mononucleosis and to provide epidemiological information on the diseases caused by EBV virus.	
Immunoglobulin Type	IgG	IgG	IgG	IgG
Sample matrix	Serum	Serum	Serum	Serum
CLIA complexity	High	High	High	High
Difference between Device and Predicate				
Antigen	EBV-VCA: VCA gp 125, affinity purified antigen	EBV-VCA: Recombinant 47 kDa fusion half of p18	EBV VCA gp25	
Strain	N/A- purified protein	N/A- Recombinant protein	N/A native protein	N/A- purified protein
Host Cell Line	EBV-VCA: Native (P_3H_3 or P_3HR-1)	EBV-VCA: E. coli (unknown)	Unknown	
Methodology	Multiplex Microbead Immunoassay (MMIA) based on Luminex XMAP technology.	Enzyme Immunoassay technology.	Multiplex bead immunoassay	Immunofluorescence Antibody (IFA) test

Item	Device	Predicates		
Name	**Plexus™ EBV IgG Multi-Analyte Diagnostics**	**Diamedix VCA IgG, ELISA**	**Athena Multi-Lyte EBV VCA IgG Test System**	**Focus Epstein-Barr Virus VCA IFA IgG**
Interpretation of test results	Perform automated calculations using Plexus software.	Manual calculation	AtheNA Multi-Lyte instrument	Manual

Comparison of Plexus EBV EBNA-1 IgG analyte to Predicate:

Item	Device	Predicate
Name	Plexus™ EBV IgG Multi-Analyte Diagnostics	Diamedix EBNA-1 IgG ELISA
Similarity between Device and Predicate		
Intended use	Focus Diagnostics' Plexus™ EBV (EBNA-1) IgG Multi-Analyte is intended for qualitatively detecting the presence or absence of human IgG class antibodies to viral capsid antigen (VCA), early antigen – diffuse pattern (EA-D), and nuclear antigen (EBNA-1) of Epstein-Barr virus (EBV) in human sera. The test is indicated as an aid in the diagnosis of EBV infection and EBV-associated infectious mononucleosis.	Diamedix Corp EBV EBNA-1 IgG ELISA is intended the qualitative and semi-quantitative determination of IgG antibodies to Epstein-Barr Virus (recombinant) Nuclear Antigen-1 (EBNA-1 IgG) in human serum by indirect enzyme immunoassay. The *Is*-EBNA-1 IgG test kit may be used in combination with other Epstein-Barr serologies, viral capsid antigen (VCA) IgG and IgM, Epstein-Barr nuclear antigen-1 (EBNA-1) IgM, early antigen-diffuse (EA-D) IgG and IgM and heterophile antibody, as an aid in the diagnosis of infectious mononucleosis (IM).
Indications for use	The test is indicated as an aid in the diagnosis of EBV infection and EBV-associated infectious mononucleosis.	The device is indicated for use with patients with the signs and symptoms of infectious mononucleosis.
Immunoglobulin Type	IgG	IgG
Sample matrix	Serum	Serum
CLIA complexity	High	High
Difference between Device and Predicate		
Strain	N/A- Recombinant protein	N/A- Recombinant protein
Antigen	EBV-EBNA: Recombinant EBNA-1, truncated, 35 kDa	EBV-EBNA-1: 27 kDa protein purified native protein (Recombinant protein)
Host Cell Line	EBV-EBNA: Pichia pastoris	EBV-EBNA: Native (unknown)

Item	Device	Predicate
Name	Plexus™ EBV IgG Multi-Analyte Diagnostics	Diamedix EBNA-1 IgG ELISA
Methodology	Multiplex Microbead Immunoassay (MMIA) based on Luminex XMAP technology.	Enzyme Immunoassay technology.
Interpretation of test results	Perform automated calculations using	Manual calculation

Comparison of Plexus EBV EA-D IgG analyte to Predicate:

Comparison to Predicate

Item	Device	Predicate
Name	Plexus™ EBV IgG Multi-Analyte Diagnostics	Diamedix EA-D IgG ELISA
Similarity between Device and Predicate		
Intended use	Focus Diagnostics' Plexus™ EBV (EA-D) IgG Multi-Analyte is intended for qualitatively detecting the presence or absence of human IgG class antibodies to viral capsid antigen (VCA), early antigen – diffuse pattern (EA-D), and nuclear antigen (EBNA-1) of Epstein-Barr virus (EBV) in human sera. The test is indicated as an aid in the diagnosis of EBV infection and EBV-associated infectious mononucleosis.	Diamedix Corp.EBV EA-D IgG ELISA is intended for the qualitative and semi-quantitative determination of IgG antibodies to Epstein-Barr Virus (recombinant) Early Antigen Diffuse (EBV-EA-D IgG) in human serum by indirect enzyme immunoassay. The *Is*-EBV-EA-D IgG test kit may be used in combination with other Epstein-Barr serologies, Viral Capsid Antigen (VCA) IgG and IgM, Epstein-Barr Nuclear Antigen-1 (EBNA-1) IgG and IgM, Early Antigen-Diffuse (EA-D) IgM and heterophile antibody, as an aid in the diagnosis of infectious mononucleosis (IM).
Indications for use	The test is indicated as an aid in the diagnosis of EBV infection and EBV-associated infectious mononucleosis.	The device is indicated for use with patients with the signs and symptoms of infectious mononucleosis.
Immunoglobulin Type	IgG	IgG
Sample matrix	Serum	Serum
CLIA complexity	High	High
Difference between Device and Predicate		
Antigen	EBV-EA: Recombinant EA-D	EBV-EA: Recombinant EA-D 28 kDa

Comparison to Predicate

Item	Device	Predicate
Name	Plexus™ EBV IgG Multi-Analyte Diagnostics	Diamedix EA-D IgG ELISA
Host Cell Line	EBV-EA: E. coli	EBV-EA: E. coli (unknown)
Strain	N/A- Recombinant protein	N/A- Recombinant protein
Methodology	Multiplex Microbead Immunoassay (MMIA) based on Luminex XMAP technology.	Enzyme Immunoassay technology.
Interpretation of test results	Perform automated calculations using Plexus software.	Manual calculation

EXPECTED VALUES

Outside investigators assessed the device with prospective masked sequential samples that were submitted for routine EBV testing (N= 723). The prevalence of EBV will vary depending on age, geographic location, testing method used and other factors. The comparator assay was performed by indirect enzyme immunoassay used in combination with other Epstein-Barr serologies (VCA) IgG and IgM, Epstein-Barr Nuclear Antigen-1 (EBNA-1) IgG, Early Antigen-Diffuse (EA-D) IgG and a heterophile rapid antibody test. The observed prevalence is in Table 1. The expected values are presented by age and gender in Tables 2-4. For all analytes, index values of <0.90 are negative, ≥0.90 to ≤ 1.10 are equivocal and > 1.10 are positives.

Table 1: Observed Prevalence - EBV Plexus

	VCA IgG	EBNA-1 IgG	EA-D IgG
Positive	66% (478/723)	50% (362/723)	17% (120/723)
Equivocal	0% (3/723)	0% (2/723)	1% (9/723)
Negative	25% (242/723)	50% (349/723)	82% (594/723)

Table 2: EBV Plexus Results VCA IgG

Age	Gender	Positive		Equivocal		Negative		
		n	%	n	%	n	%	
<5	F	8	53.3	0	0.0	7	46.7	15
<5	M	17	47.2	0	0.0	19	52.8	36
5-12	F	43	43.0	1	1.0	56	56.0	100
5-12	M	46	48.4	0	0.0	49	51.6	95
13-20	F	118	70.7	0	0.0	49	29.3	167
13-20	M	82	63.1	1	0.8	47	36.2	130
21-30	F	37	97.4	0	0.0	1	2.6	38
21-30	M	15	83.3	0	0.0	3	16.7	18
31-40	F	14	87.5	0	0.0	2	12.5	16
31-40	M	13	92.9	0	0.0	1	7.1	14

Table 2: EBV Plexus Results VCA IgG								
Age	Gender	Positive		Equivocal		Negative		
		n	%	n	%	n	%	
41-50	F	19	100	0	0.0	0	0.0	19
41-50	M	12	92.3	0	0.0	1	7.7	13
51-60	F	15	93.8	0	0.0	1	6.3	16
51-60	M	8	72.7	0	0.0	3	27.3	11
61-70	F	9	100	0	0.0	0	0.0	9
61-70	M	8	80.0	0	0.0	2	20.0	10
>70	F	7	100	0	0.0	0	0.0	7
>70	M	7	77.8	1	11.1	1	11.1	9
Total		478	66.1	3	0.4	242	33.5	723

Table 3: EBV Plexus Results EBNA-1 IgG								
			Positive		Equivocal		Negative	
Age	Gender	n	%	n	%	n	%	Total
<5	F	3	20.0	0	0.0	12	80.0	15
<5	M	12	33.3	0	0.0	24	66.7	36
5-12	F	28	28.0	0	0.0	72	72.0	100
5-12	M	36	37.9	1	1.1	58	61.1	95
13-20	F	85	50.9	0	0.0	82	49.1	167
13-20	M	52	40.0	0	0.0	78	60.0	130
21-30	F	27	71.1	0	0.0	11	28.9	38
21-30	M	10	55.6	0	0.0	8	44.4	18
31-40	F	15	93.8	0	0.0	1	6.3	16
31-40	M	11	78.6	0	0.0	3	21.4	14
41-50	F	17	89.5	0	0.0	2	10.5	19
41-50	M	10	76.9	0	0.0	3	23.1	13
51-60	F	16	100.0	0	0.0	0	0.0	16
51-60	M	10	90.9	0	0.0	1	9.1	11
61-70	F	9	100.0	0	0.0	0	0.0	9
61-70	M	8	80.0	0	0.0	2	20.0	10
>70	F	6	85.7	0	0.0	1	14.3	7
>70	M	7	77.8	1	11.1	1	11.1	9
Total		362	50.1	2	0.3	359	49.7	723

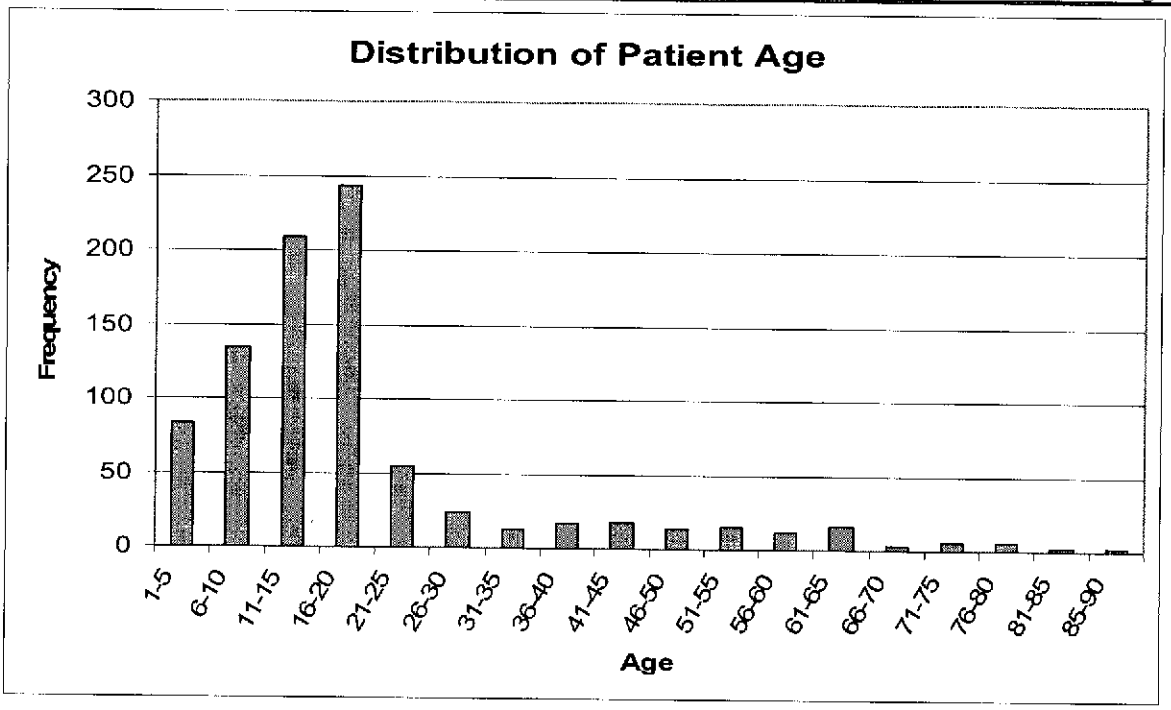
Table 4: EBV Plexus Results EA-D IgG

		Positive		Equivocal		Negative		
Age	Gender	n	%	n	%	n	%	Total
<5	F	1	6.7	1	6.7	13	86.7	15
<5	M	4	11.1	0	0.0	32	88.9	36
5-12	F	11	11.0	0	0.0	89	89.0	100
5-12	M	9	9.5	1	1.1	85	89.5	95
13-20	F	27	16.2	2	1.2	138	82.6	167
13-20	M	25	19.2	2	1.5	103	79.2	130
21-30	F	9	23.7	0	0.0	29	76.3	38
21-30	M	5	27.8	0	0.0	13	72.2	18
31-40	F	5	31.3	0	0.0	11	68.8	16
31-40	M	2	14.3	0	0.0	12	85.7	14
41-50	F	5	26.3	1	5.3	13	68.4	19
41-50	M	1	7.7	1	7.7	11	84.6	13
51-60	F	3	18.8	0	0.0	13	81.3	16
51-60	M	3	27.3	1	9.1	7	63.6	11
61-70	F	4	44.4	0	0.0	5	55.6	9
61-70	M	3	30.0	0	0.0	7	70.0	10
>70	F	3	42.9	0	0.0	4	57.1	7
>70	M	0	0.0	0	0.0	9	100.0	9
Total		120	16.6%	9	1.2%	594	82.2%	723

The table below summarizes the breakdown of the samples age and gender information. The distribution chart below exhibits the age distribution of all 873 samples included in the study.

Age Information:

Summary of Female Subjects		Summary of Male Subjects	
n	474	n	399
mean	20.0	mean	18.3
median	16.0	median	14.0
min	1	min	1
max	88	max	87



PERFORMANCE CHARACTERISTICS

Typical Antibody Response Classification

The table below summarizes a generally accepted algorithm for classifying the EBV infection status via EBV serologic profiles. For acute EBV serological status, both EBV IgM and EBV IgG antibodies to viral capsid antigen (VCA) rise rapidly. EBV VCA IgM antibody disappears over approximately four weeks. Heterophile antibody, (IgM class), appears only during acute infection and fades rapidly over approximately four weeks. EBV EA-D IgG antibody shows a translent raise during acute infections and is undetectable after three to six months. EBV EBNA-1 IgG antibody usually appears three months after initial infection and remains for life. The serological status was determined by the use of commercially available ELISA assays for the EBV analytes EBNA-1 IgG, VCA IgG, EA-D IgG and VCA IgM. A commercially available heterophile rapid test was used to determine the analyte status of the Heterophile antibody.

EBV Serological Status		EBNA-1 IgG	EBV VCA IgG	EBV EA-D IgG	EBV VCA IgM	Heterophile Antibody
Acute	Primary Acute	Negative	Negative	Negative	Positive	Negative
		Negative	Negative	Negative	Positive	Positive
		Negative	Positive	Negative	Positive	Positive
		Negative	Negative	Positive	Positive	Negative
		Negative	Negative	Positive	Positive	Positive
		Negative	Positive	Positive	Positive	Negative
		Negative	Positive	Positive	Positive	Positive
		Negative	Positive	Positive	Negative	Positive
	Late Acute	Positive	Positive	Positive	Negative	Negative
		Positive	Positive	Positive	Positive	Positive
		Positive	Positive	Positive	Positive	Negative
		Positive	Positive	Negative	Positive	Positive
		Positive	Positive	Negative	Positive	Negative
		Negative	Positive	Negative	Positive	Negative
Recovering		Negative	Positive	Positive	Negative	Negative
Past Infection		Negative	Positive	Negative	Negative	Negative
		Positive	Positive	Negative	Negative	Negative
No Infection		Negative	Negative	Negative	Negative	Negative
Indeterminant		Combinations not listed above (n =18)				

Comparison Studies

Performance of the Plexus EBNA-1 IgG and Plexus EA-D IgG analytes were tested against a commercially available ELISA test whereas performance of the Plexus EBV VCA IgG analyte was tested against a combination (hereafter referred to as 'consensus predicate') of a FDA-cleared commercially available ELISA, a FDA cleared commercially available immunofluroscent (IFA) test and a FDA cleared commercially available flow cytometry based immunoassay. For each sample, a consensus based algorithm (2/3) was used to determine the predicate result for comparison with the Plexus VCA IgG result. The studies were conducted at three United States testing sites: a hospital laboratory located in Northeast, a pediatric hospital laboratory located in the Mid-West, and Focus with serum samples in which EBV tests were ordered. The sera were sequentially submitted to the laboratory, archived, and masked. Samples were collected at three sites and include both prospective (n = 723) and retrospective (n = 150) specimens. Retrospective samples were pre-selected based on EBV VCA IgM positive results from a FDA cleared device. Results are summarized by analyte.

EBV VCA IgG vs Consensus Predicate: Comparison by Serological Status (Prospective Population Samples N = **723**)

Samples were collected and tested by the Northeast investigator (n = 350), Mid-West investigator (n=249) and Focus (n=124).

The following table outlines the positive and negative percent agreements across various serological classifications for prospective samples for VCA IgG analyte when the consensus predicate is used for VCA IgG analysis. Serological status was determined by the use of commercially available ELISA assays for the EBV analytes EBNA-1 IgG, VCA IgG, EA-D IgG and VCA IgM and a commercially available heterophile rapid test for the Heterophile antibody.

Table 4: EBV VCA IgG Results

		Consensus Predicate		Plexus			
Serostatus by Predicates			**n**	**Positive**	**Equivocal**	**Negative**	**% Agreement**
Acute	Primary Acute	Positive	57	57	0	0	100%(57/57), 95% CI:93.7-100%
		Negative	1	0	0	1	33.3%(1/3), 95% CI:6.1-79.2%
		No consensus[1]	2	2	0	0	NA
	Late Acute	Positive	72	70	1	1	97.2%(70/72), 95% CI:90.4-99.2%
		Negative	0	0	0	0	NA
		No consensus	0	0	0	0	NA
Recovering		Positive	1	1	0	0	100%(1/1), 95% CI:20.7-100%
		Negative	0	0	0	0	NA
		No consensus	0	0	0	0	NA
Previous Infection		Positive	292	282	1	9	96.6%(282/292), 95% CI:93.8-98.1%
		Negative	6	1	0	5	83.3%(5/6), 95% CI:43.6-97%
		No consensus	0	0	0	0	NA
No Infection		Positive	9	3	0	6	30%(3/10), 95% CI:10.8-60.3%
		Negative	217	13	1	203	93.5%(203/217), 95% CI:89.5-96.1%
		No consensus[1]	1	0	0	1	NA
Indeterminate		Positive	50	49	0	1	98%(49/50), 95% CI:89.5-99.6%
		Negative	15	0	0	15	100%(15/15),95% CI:79.6-100%
		No consensus	0	0	0	0	NA

[1] No consensus results: the combination of three predicates could not yield a conclusive result for these samples – a 2/3 majority could not be obtained.

EBV EBNA-1 vs Predicate: Comparison by Serological Status (Prospective Population Samples N = **723**)

Samples were collected and tested by the Northeast investigator (n = 350), Mid-West investigator (n=249) and Focus (n=124).

The following table outlines the positive and negative percent agreements across various serological classifications for prospective samples for EBNA-1 IgG analyte when a commercial ELISA test is used as a predicate for EBNA-1 IgG analysis. Serological status was determined by the use of commercially available ELISA assays for the EBV analytes EBNA-1 IgG, VCA IgG, EA-D IgG and VCA IgM and a commercially available heterophile rapid test for the Heterophile antibody.

Table 5: EBV EBNA-1 IgG Results

		Predicate ELISA		Plexus			
Serological Status by Predicates			**n**	**Positive**	**Equivocal**	**Negative**	**% Agreement**
Acute	Primary Acute	Positive	0	0	0	0	NA
		Equivocal	0	0	0	0	NA
		Negative	60	0	0	60	100%(60/60), 95% CI:94-100%
	Late Acute	Positive	69	65	0	4	94.2%(65/69), 95% CI:86-97.7%
		Equivocal	0	0	0	0	NA
		Negative	3	0	0	3	100%(3/3), 95% CI:43.8-100%
Recovering		Positive	0	0	0	0	NA
		Equivocal	0	0	0	0	NA
		Negative	1	0	0	1	100%(1/1), 95% CI:20.7-100%
Previous Infection		Positive	284	266	2	16	93.7%(266/284), 95% CI:90.2-96%
		Equivocal	0	0	0	0	NA
		Negative	14	1	0	13	92.9%(13/14), 95% CI:68.5-98.7%
No Infection		Positive	0	0	0	0	NA
		Equivocal	0	0	0	0	NA
		Negative	227	1	0	226	99.6%(226/227), 95% CI:97.5-99.9%
Indeterminate		Positive	36	29	0	7	76.3%(29/38), 95% CI:60.8-87%
		Equivocal	2	0	0	2	0%(0/2), 95% CI:0-65.8%
		Negative	27	0	0	27	100%(27/27), 95% CI:87.5-100%

EBV EA-D vs Predicate: Comparison by Serological Status (Prospective Population Samples N = **723**)
Samples were collected and tested by the Northeast investigator (n = 350), Mid-West investigator (n=249) and Focus (n=124).

The following table outlines the positive and negative percent agreements across various serological classifications for prospective samples for EA-D IgG analyte when a commercial ELISA test is used as a predicate for EA-D IgG analysis. Serological status was determined by the use of commercially available ELISA assays for the EBV analytes EBNA-1 IgG, VCA IgG, EA-D IgG and VCA IgM and a commercially available heterophile rapid test for the Heterophile antibody.

Table 6: EBV EA-D IgG Results

		Predicate ELISA		Plexus			
Serological Status by Predicates			**n**	**Positive**	**Equivocal**	**Negative**	**% Agreement**
Acute	Primary Acute	Positive	43	40	0	3	93%(40/43), 95% CI:81.4-97.6%
		Equivocal	0	0	0	0	NA
		Negative	17	4	0	13	76.5%(13/17), 95% CI:52.7-90.4%
	Late Acute	Positive	51	41	1	9	80.4%(41/51), 95% CI:67.5-89%
		Equivocal	0	0	0	0	NA
		Negative	21	2	2	17	81%(17/21), 95% CI:60-92.3%
Recovering		Positive	1	0	0	1	0%(0/1), 95% CI:0-79.3%
		Equivocal	0	0	0	0	NA
		Negative	0	0	0	0	NA
Previous Infection		Positive	0	0	0	0	NA
		Equivocal	0	0	0	0	NA
		Negative	298	11	1	286	96%(286/298), 95% CI:93.1-97.7%
No Infection		Positive	0	0	0	0	NA
		Equivocal	0	0	0	0	NA
		Negative	227	1	3	223	98.2%(223/227), 95% CI:95.6-99.3%
Indeterminate		Positive	12	7	0	5	26.9%(7/26), 95% CI:13.7-46.1%
		Equivocal	30	14	2	14	6.3%(2/32), 95% CI:1.7-20.1%
		Negative	23	0	0	23	62.2%(23/37), 95% CI:46.1-75.9%

EBV VCA IgG vs Consensus Predicate: Comparison by Serological Status (Retrospective Presumed Acute Population Samples N = 150)

Samples were collected and tested by Mid-West investigator (n=150).

The following table outlines the positive and negative percent agreements across various serological classifications for retrospective samples for VCA IgG analyte when the consensus predicate is used for VCA IgG analysis. Serological status was determined by the use of commercially available ELISA assays for the EBV analytes EBNA-1 IgG, VCA IgG, EA-D IgG and VCA IgM and a commercially available heterophile rapid test for the Heterophile antibody.

Table 7: EBV VCA IgG Results

		Consensus Predicate		Plexus			
Serostatus by Predicates			**n**	**Positive**	**Equivocal**	**Negative**	**% Agreement**
Acute	Primary Acute	Positive	106	99	1	6	93.4%(99/106), 95% CI:87-96.8%
		Negative	0	0	0	0	NA
		No consensus	0	0	0	0	NA
	Late Acute	Positive	8	8	0	0	100%(8/8), 95% CI:67.6-100%
		Negative	0	0	0	0	NA
		No consensus	0	0	0	0	NA
No Infection		Positive	1	1	0	0	100%(1/1), 95% CI:20.7-100%
		Negative	1	1	0	0	0%(0/1), 95% CI:0-79.3%
		No consensus	0	0	0	0	NA
Indeterminate		Positive	33	31	0	2	93.9%(31/33), 95% CI:80.4-98.3%
		Negative	0	0	0	0	NA
		No consensus[1]	1	1	0	0	NA

[1] No consensus results: the combination of three predicates could not yield a conclusive result for these samples – a 2/3 majority could not be obtained.

EBV EBNA-1 vs Predicate: Comparison by Serological Status (Retrospective Presumed Acute Population Samples N = 150)
Samples were collected and tested by Mid-West investigator (n=**150**).

The following table outlines the positive and negative percent agreements across various serological classifications for retrospective samples for EBNA-1 IgG analyte when a commercial ELISA test is used as a predicate for EBNA-1 IgG analysis. Serological status was determined by the use of commercially available ELISA assays for the EBV analytes EBNA-1 IgG, VCA IgG, EA-D IgG and VCA IgM and a commercially available heterophile rapid test for the Heterophile antibody.

Table 8: EBV EBNA-1 IgG Results

		Predicate ELISA		Plexus			
Serological Status by Predicates			**n**	**Positive**	**Equivocal**	**Negative**	**% Agreement**
Acute	Primary Acute	Positive	0	0	0	0	NA
		Equivocal	0	0	0	0	NA
		Negative	106	1	0	105	99.1%(105/106), 95% CI:94.8-99.8%
	Late Acute	Positive	4	0	0	4	0%(0/4), 95% CI:0-49%
		Equivocal	0	0	0	0	NA
		Negative	4	0	0	4	100%(4/4), 95% CI:51-100%
No Infection		Positive	0	0	0	0	NA
		Equivocal	0	0	0	0	NA
		Negative	2	0	0	2	100%(2/2), 95% CI:34.2-100%
Indeterminate		Positive	4	0	0	4	0%(0/8), 95% CI:0-32.4%
		Equivocal	4	0	0	4	0%(0/4), 95% CI:0-49.0%
		Negative	26	0	0	26	100%(26/26), 95% CI:87.1-100%

EBV EA-D vs Predicate: Comparison by Serological Status (Retrospective Presumed Acute Population Samples N = 150)
Samples were collected and tested by Mid-West investigator (n=150).

The following table outlines the positive and negative percent agreements across various serological classifications for retrospective samples for EA-D IgG analyte when a commercial ELISA test is used as a predicate for EA-D IgG analysis. Serological status was determined by the use of commercially available ELISA assays for the EBV analytes EBNA-1 IgG, VCA IgG, EA-D IgG and VCA IgM and a commercially available heterophile rapid test for the Heterophile antibody.

Table 9: EBV EA-D IgG Results

		Predicate ELISA		Plexus			
Serological Status by Predicates			**n**	**Positive**	**Equivocal**	**Negative**	**% Agreement**
Acute	Primary Acute	Positive	61	57	1	3	93.4%(57/61), 95% CI:84.3-97.4%
		Equivocal	0	0	0	0	NA
		Negative	45	7	3	35	77.8%(35/45), 95% CI:63.7-87.5%
	Late Acute	Positive	3	3	0	0	100%(3/3), 95% CI:43.8-100%
		Equivocal	0	0	0	0	NA
		Negative	5	1	0	4	80%(4/5), 95% CI:37.6-96.4%
No Infection		Positive	0	0	0	0	NA
		Equivocal	0	0	0	0	NA
		Negative	2	0	0	2	100%(2/2), 95% CI:34.2-100%
Indeterminate		Positive	10	8	0	2	66.7%(8/12), 95% CI:39.1-86.2%
		Equivocal	14	12	0	2	0%(0/14), 95% CI:0-21.5%
		Negative	10	0	1	9	40.9%(9/22), 95% CI:23.3-61.3%

Inter-laboratory, Intra-assay and Inter-assay Reproducibility

The inter/intra-assay reproducibility and the inter-laboratory reproducibility testing were performed at three laboratories. Each of the three laboratories tested twelve samples in triplicate on five different days. The results of the study are summarized in the table below.

Table 16: Inter-laboratory, Intra-assay and Inter-assay Reproducibility

Plexus VCA IgG						Plexus EBNA IgG						Plexus EA IgG					
ID	Intra-assay & Inter-assay %CV			Inter-Lab		ID	Intra-assay & Inter-assay %CV			Inter-Lab		ID	Intra-assay & Inter-assay %CV			Inter-Lab	
	Mean Index	Intra-assay	Inter-assay	Mean Index	% CV		Mean Index	Intra-assay	Inter-assay	Mean Index	% CV		Mean Index	Intra-assay	Inter-assay	Mean Index	% CV
5	5.38	2.1%	8.1%	5.38	7.4%	12	6.66	2.1%	8.7%	6.66	8.9%	12	4.42	3.9%	7.5%	4.42	2.0%
19	5.12	2.9%	10.0%	5.12	10.1%	15	4.41	4.1%	6.9%	4.42	5.0%	4	2.69	3.6%	19.9%	2.69	7.0%
20	5.02	2.4%	8.4%	5.03	8.1%	8	3.66	2.5%	6.7%	3.66	5.8%	16	1.88	4.7%	7.5%	1.88	4.7%
6	4.21	3.2%	6.7%	4.20	3.7%	4	2.68	5.6%	18.3%	2.67	7.8%	15	1.39	5.6%	15.6%	1.39	15.7%
4	3.37	4.3%	16.6%	3.37	2.5%	18	2.05	3.8%	9.0%	2.05	8.6%	19	0.99	6.0%	12.0%	0.99	7.9%
16	2.21	4.1%	28.4%	2.22	27.0%	5	1.84	3.7%	8.0%	1.84	4.8%	8	0.91	3.7%	8.6%	0.91	2.1%
18	2.11	4.0%	6.0%	2.11	3.7%	6	1.47	5.1%	11.8%	1.46	11.7%	5	0.76	4.7%	12.6%	0.76	5.6%
2	2.01	3.9%	7.9%	2.01	4.4%	2	1.00	4.0%	13.4%	1.00	13.6%	20	0.63	5.3%	8.5%	0.63	2.6%
11	1.16	6.3%	13.3%	1.16	11.9%	3	0.81	6.1%	16.0%	0.81	11.9%	18	0.32	5.3%	9.6%	0.32	6.6%
8	1.11	4.7%	77.0%	1.12	31.1%	16	0.77	6.1%	59.1%	0.77	50.9%	6	0.29	6.1%	33.8%	0.29	4.7%
15	0.38	8.7%	19.6%	0.38	13.4%	20	0.65	5.4%	11.1%	0.65	8.9%	2	0.21	5.2%	61.9%	0.21	12.4%
1	0.17	18.2%	69.2%	0.17	59.3%	9	0.15	9.8%	304.1%	0.15	134%	3	0.21	8.2%	64.6%	0.21	10.1%
9	0.11	15.2%	117.9%	0.11	72.5%	19	0.11	7.8%	23.8%	0.11	19.8%	11	0.18	6.6%	106.1%	0.18	27.0%
3	1.71	5.4%	11.4%	1.71	5.8%	1	0.07	14.0%	41.1%	0.07	34.7%	1	0.15	9.1%	96.5%	0.15	16.9%
12	4.69	2.6%	7.7%	4.69	5.4%	11	0.04	11.2%	32.9%	0.04	23.1%	9	0.10	8.0%	40.1%	0.10	28.1%

Inter-Lot Reproducibility

The inter-lot reproducibility was evaluated with fifteen (15) samples in triplicates on three (3) lots of Plexus EBV kit. The results of the study are summarized in the table below.

Table 10: Inter-lot Reproducibility

Plexus VCA IgG			Plexus EBNA IgG			Plexus EA-D IgG		
ID	Mean	%CV	ID	Mean	%CV	ID	Mean	%CV
5	6.00	3.2%	12	7.35	3.6%	12	4.51	5.3%
19	5.88	2.3%	15	4.76	4.6%	4	2.86	3.3%
20	5.57	2.4%	8	4.01	4.5%	16	1.84	2.0%
12	5.08	3.7%	4	2.62	4.8%	15	1.36	9.0%
6	4.66	3.3%	18	2.39	6.7%	19	1.00	4.6%
4	3.61	1.3%	5	1.66	3.5%	8	0.85	7.2%
18	2.08	3.7%	6	1.44	5.8%	5	0.68	4.8%
2	2.01	2.4%	2	0.93	5.0%	20	0.59	2.3%
16	1.77	4.8%	3	0.74	2.3%	18	0.30	8.6%
3	1.72	4.0%	20	0.58	3.5%	6	0.29	4.2%
11	1.00	3.8%	16	0.36	3.2%	2	0.21	8.3%
8	0.75	2.8%	19	0.10	7.7%	3	0.20	5.8%
15	0.31	7.8%	1	0.06	5.7%	11	0.18	14.4%
1	0.11	7.7%	11	0.04	8.1%	1	0.15	10.8%
9	0.02	0.0%	9	0.02	30.0%	9	0.11	6.4%

Cross-Reactivity

A cross-reactivity study was performed to determine if samples from various disease states and other potentially cross-reactivity factors interfere with test results when tested with the Plexus EBV IgG kit. A panel of (ANA= 28, CMV= 31, HSV-1= 29, HSV-2=13, HSV-6= 4, Rubeola Virus =1, Mumps = 1, Rubella Virus=39, *Toxoplasma gondii* =19, and VZA= 35) samples for each cross reactant were evaluated for possible cross reactivity with the Plexus EBV IgG kit for each of the three (VCA, EA-D and EBNA-1) IgG analyte. Of the 107 samples tested, 41 were prescreened for EBV IgG negativity. Because of the high prevalence of EBV IgG antibodies in the normal population, the test samples were also evaluated on commercially available ELISA. The majority of all samples that did elicit a positive result were also confirmed positive by the corresponding commercially available ELISA, indicating reactivity to EBV IgG antibodies rather than cross reactivity with a potentially interfering factor.

Table 11: Cross-Reactivity

Cross Reactives	N	Method	EBV VCA IgG			EBV EBNA IgG			EBV EAD IgG		
			Positive	Equivocal	Negative	Positive	Equivocal	Negative	Positive	Equivocal	Negative
ANA	28	Plexus	27	0	1	28	0	0	8	0	20
		ELISA	28	0	0	28	0	0	5	5	18
		Discrepants	1			0			6^5		
Cytomegalovirus (CMV)	31	Plexus	24	1	6	24	0	7	4	0	27
		ELISA	26	0	5	25	0	6	3	1	27
		Discrepants	2^1			1			2^1		
HSV-1	29	Plexus	27	1	1	26	0	2	3	1	25
		ELISA	27	0	2	28	1	1	3	0	26
		Discrepants	2^1			2^1			1^1		
HSV-2	13	Plexus	13	0	0	12	0	1	2	3	8
		ELISA	13	0	0	13	0	0	2	1	10
		Discrepants	0			1			4^4		
HHV-6	4	Plexus	0	0	4	0	0	4	0	0	4
		ELISA	0	0	4	0	0	4	0	0	4
		Discrepants	0			0			0		
Measles (Rubeola)	1	Plexus	0	0	1	0	0	1	0	0	1
		ELISA	0	0	1	0	0	1	0	0	1
		Discrepants	0			0			0		

Table 11: Cross-Reactivity

Cross Reactives	N	Method	EBV VCA IgG			EBV EBNA IgG			EBV EAD IgG		
			Positive	Equivocal	Negative	Positive	Equivocal	Negative	Positive	Equivocal	Negative
Mumps	1	Plexus	0	0	1	0	0	1	0	0	1
		ELISA	0	0	1	0	0	1	0	0	1
		Discrepants	0			0			0		
Rubella Virus	39	Plexus	26	0	13	25	1	13	4	1	34
		ELISA	26	1	12	27	0	12	3	2	34
		Discrepants	8[1]			2[1]			1[1]		
Toxoplasma gondii	19	Plexus	17	0	2	18	0	1	1	4	14
		ELISA	19	0	0	18	0	1	1	2	16
		Discrepants	2			0			4[4]		
Varicella-zoster (VZV)	35	Plexus	26	0	9	22	0	13	4	1	30
		ELISA	24	0	11	22	0	13	4	2	29
		Discrepants	4			0			4[3]		

[1]One Equivocal Sample; [2]Two Equivocal Samples; [3]Three Equivocal Samples; [4]Four Equivocal Samples; [5]Five Equivocal Samples

Sample Storage and Handling

Fifteen (15) negative and positive for EBV IgG samples were used to assess the reactivity of unfrozen sample against samples that were frozen and thawed for up to five cycles. No effect was observed for any of the freeze-thaw cycling in either the positive or negative sample.

Interference

The test performance was evaluated with the presence of interfering substances. Four samples, two positive and two negative for EBV IgG antibodies by Plexus EBV IgG were used in the study. Baseline levels for triglycerides, albumin, bilirubin, and hemoglobin were established for each sample. The remaining serum was spiked with purchased interfering substances at levels that exceeded the expected human range. The spiked samples were tested again in the assay to determine if the elevated levels of interfering substances affected the assay. No interference was observed for any of the interfering substances in either the positive or negative sample.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Focus Diagnostics, Inc.
C/O Constance Bridges
10703 Progress Way
Cypress, California 90630

JUL 2 8 2008

Re: k073382
Trade/Device Name: Plexus EBV IgG Multi-Analyte Diagnostics
Regulation Number: 21 CFR 866.3235
Regulation Name: Epstein-Barr Virus Serological Device
Regulatory Class: Class I
Product Code: LSE
Dated: November 30, 2007
Received: December 3, 2007

Dear Ms. Bridges:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at 240-276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): K073382

Device Name: Plexus EBV IgG Multi-Analyte Diagnostics

Indications for Use: Focus Diagnostics' Plexus™ EBV IgG Multi-Analyte Diagnostics test kit is intended for qualitatively detecting the presence or absence of human IgG class antibodies to viral capsid antigen (VCA), early antigen- diffuse (EA-D), and nuclear antigen (EBNA-1) of Epstein-Barr virus in human sera. The test is indicated as an aid in the diagnosis of EBV infection and EBV-associated infectious mononucleosis.

The performance of this assay has not been established for use in the diagnosis of nasopharyngeal carcinoma and Burkitt's lymphoma, for testing of immunocompromised patients, for use by a point of care facility or for use with automated equipment. This assay has not been evaluated for donor screening.

Prescription Use __X__ AND/OR Over-the-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k) K073382